



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Tsunehiro FUKUCHI et al.:

Serial No. 10/522,603:

Art Unit: 1655

Filed: January 26, 2005:

Examiner: Catheryne CHEN

5 For: CHINESE HERBAL MEDICAL COMPOSITION IN THE FORM OF
JELLY

DECLARATION

Honorable Commissioner for Patents

Sir:

10 I, Tsunehiro FUKUCHI, a citizen of Japan residing in A201, East
16, 541, Kirai, Higashikagawa-shi, Kagawa-ken, Japan, declare as
follows:

I graduated from Kagawa University, Department of Education in
1991, and graduated Kyushu Institute of Technology, School of
15 Computer Science and System Engineering in 1994.

From 1994 to now, I have been employed in TEIKOKU SEIYAKU
CO., LTD. and I have engaged in research and development on the
preparation of Chinese medicines in said company.

I am one of inventors of the above patent application (U.S. Serial
20 No. 10/522,603) and am familiar with subject matter thereof.

Under my supervision the following tests were carried out.

The following experiments were carried out experiments to
confirm whether or not the preparation containing a Chinese herbal
25 medicine according to Fukui et al. (U.S. Patent 6,277,395 B1) is

for long term preservation.

1. Samples for tests

A manufacturing method of samples:

- 5 Each ingredient shown in the following Tables was weighed, and the ingredients were homogenously mixed and stirred, followed by addition of water. The mixture was stirred and dissolved under heating at 80°C for 1 hour. The solution was instantly poured into a stick-like vessel and then was left at 20 to 25°C for more than 12 hours to solidify.
- 10 Sample A: having the same ingredients as example 2 of the present invention.

Samples a, b and c: being prepared by mixing Chinese herbal medicine, Kakkonto to ingredients of Embodiment 1 of Fukui et al.

15 Table 1

| | Sample a | Sample b | Sample c |
|--|----------|----------|----------|
| Aqueous dry extract of Kakkon-to (葛根湯) | 30.00 | 15.00 | 15.00 |
| Agar | 0.20 | 0.20 | 0.20 |
| Locust bean gum | 0.05 | 0.05 | 0.05 |
| Pectin | 0.04 | 0.04 | 0.04 |
| Carrageenan (ι) | 0.02 | 0.02 | - |
| Carrageenan (κ) | - | - | 0.02 |
| Xanthangum | 0.01 | 0.01 | 0.01 |
| Citric acid | 0.21 | 0.21 | 0.21 |
| Trisodium citrate | 0.14 | 0.14 | 0.14 |
| Erythritol | 8.82 | 8.82 | 8.82 |
| Flavor | - | - | - |
| Purified water | 60.51 | 75.51 | 75.51 |
| Total | 100.00 | 100.00 | 100.00 |

Table 2

| | Sample A |
|--|----------|
| Aqueous dry extract of Kakkon-to (葛根湯) | 15 |
| Carrageenan (1) | 1 |
| Locust bean gum (Carob bean gum) | 0.25 |
| Xanthangum | 0.45 |
| Powdered hydrogenated maltose starch syrup | 6 |
| D-Sorbitol | 6 |
| Glycerin | 6 |
| Propylene glycol | 1 |
| Propyl parahydroxybenzoate | 0.02 |
| Purified water | 64.28 |
| Total | 100.00 |

2. Stability Test

(1) Syneresis

- 5 The preparation kept at 25°C 60%RH and by standing on end of the stick-like vessel containing a sample was used for this test.
- After previously weighted the weight of metal gauze with mesh size of 355μm and the weight of soft paper for absorbing water separated from the sample, the paper folded up was put under the metal gauze. The
- 10 stick-like vessel was opened and its content (sample) was put on the metal gauze.
- Separated water was absorbed with the paper under the metal gauze taking 1 minute. The weights of the metal gauze with the sample and the paper containing the separated water were measured. Amount (%)
- 15 of separated water (syneresis) was calculated from the above measured weights.

The results are shown in Table 3.

Observation

The preparation of Sample A of the present invention hardly shows syneresis. On the other hand, syneresis on Samples a, b and c of Fukui et al. were very great and these Samples can not be used for long term preservation.

Table 3

| 25°C 60%RH | Initial value * | | After 10 days | | After 67 days | |
|---------------|-----------------|---------------|---------------|---------------|---------------|---------------|
| Sample a | 3.82 | $\pm(2.33)\%$ | 25.20 | $\pm(0.28)\%$ | 37.86 | $\pm(7.33)\%$ |
| Sample b | 35.22 | $\pm(2.26)\%$ | 35.91 | $\pm(3.26)\%$ | 31.37 | $\pm(5.88)\%$ |
| Sample c | 18.28 | $\pm(0.70)\%$ | 21.90 | $\pm(0.93)\%$ | 29.03 | $\pm(2.75)\%$ |
| Sample A | 0.02 | $\pm(0.02)\%$ | 0.04 | $\pm(0.03)\%$ | 0.17 | $\pm(0.08)\%$ |

* One day after manufacturing the sample, the value which was measured on the sample was as initial value.

The results shown in Table 3 are also shown in following figures (Fig. 1 to 2).

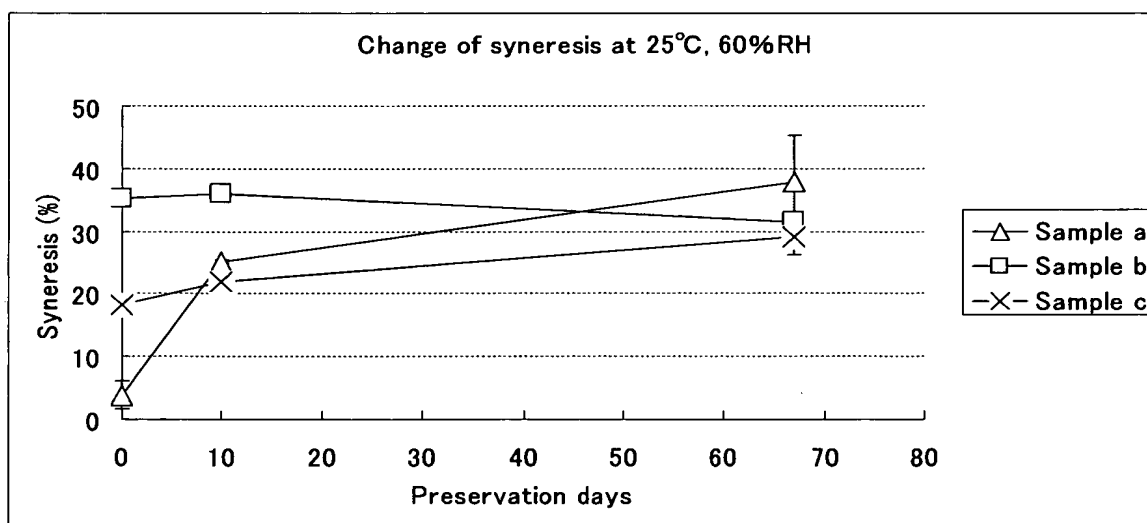


Fig. 1

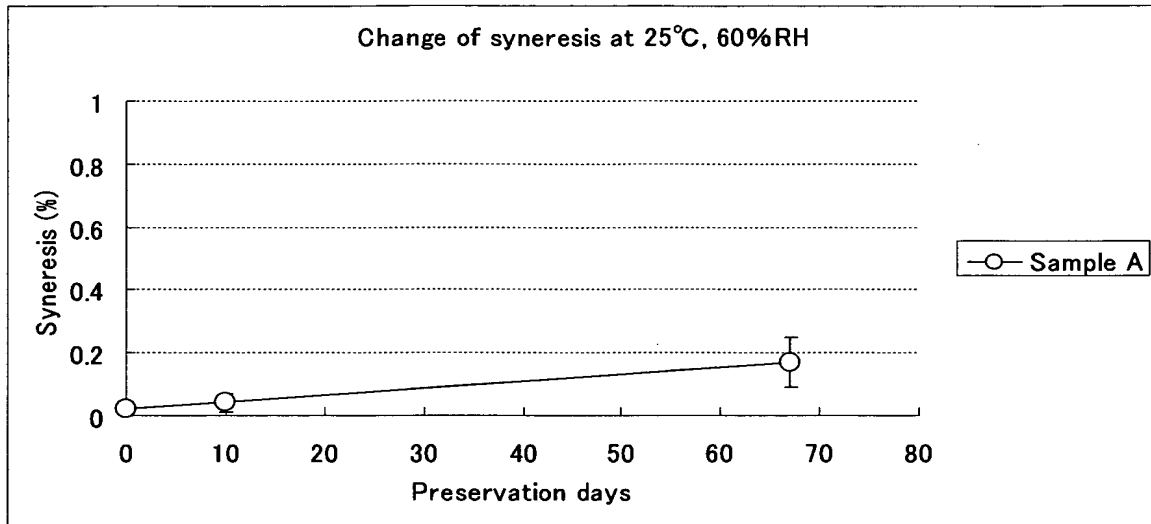


Fig. 2

5 (2) Change of breaking load (strength of gel)

The test was carried out using an equipment shown in attachment.

Equipment for measurement: Creep meter (Yamaden Co.)

After putting a Sample into a plastic Petri dish (Diameter: 51mm, Height: 9mm), the dish was covered with a lid and covered around the dish with parafilm (Laboratory film: ALCAN) for protecting spatter of the water and then the test was carried out.

Samples which had kept at 40°C 75%RH and 25°C 60%RH were take out and said samples were kept at $20 \pm 3^\circ\text{C}$ for about 6 to 12 hours for preconditioning, the test on the samples was carried out under the following condition.

Plunger diameter: 1cm, height: 3cm, compression speed: 1mm/sec

Clearance 45%, measured temperature: $20 \pm 3^\circ\text{C}$

The maximum breaking load was measured as strength.

The results were shown in following Tables 4 and 5.

Table 4

| 25°C 60%RH | Initial value * | | After 5 days | | After 10 days | |
|---------------|-----------------|----------------|--------------|-----------------|---------------|-----------------|
| Sample a | 3.40 | $\pm(1.18)$ gf | 4.42 | $\pm(0.59)$ gf | 4.76 | $\pm(0.59)$ gf |
| Sample b | 4.76 | $\pm(2.57)$ gf | 2.72 | $\pm(0.59)$ gf | 3.40 | $\pm(0.59)$ gf |
| Sample c | 6.46 | $\pm(0.59)$ gf | 6.12 | $\pm(0.00)$ gf | 6.12 | $\pm(0.00)$ gf |
| Sample A | 208.02 | $\pm(5.40)$ gf | 196.13 | $\pm(14.29)$ gf | 180.15 | $\pm(36.50)$ gf |

Table 5

| 40°C 75%RH | Initial value * | | After 5 days | | After 10 days | |
|---------------|-----------------|----------------|--------------|-----------------|---------------|----------------|
| Sample a | 3.40 | $\pm(1.18)$ gf | 5.78 | $\pm(0.59)$ gf | 5.44 | $\pm(0.59)$ gf |
| Sample b | 4.76 | $\pm(2.57)$ gf | 3.06 | $\pm(0.00)$ gf | 2.04 | $\pm(0.00)$ gf |
| Sample c | 6.46 | $\pm(0.59)$ gf | 6.12 | $\pm(0.00)$ gf | 5.10 | $\pm(0.00)$ gf |
| Sample A | 208.02 | $\pm(5.40)$ gf | 234.88 | $\pm(26.68)$ gf | 200.20 | $\pm(5.62)$ gf |

* One day after manufacturing the sample, the value which was measured on the sample was as initial value.

The above results are also shown in Fig. 3 to 6.

Observation

- 5 Gel strength on every sample was hardly changed for preservation for long term.

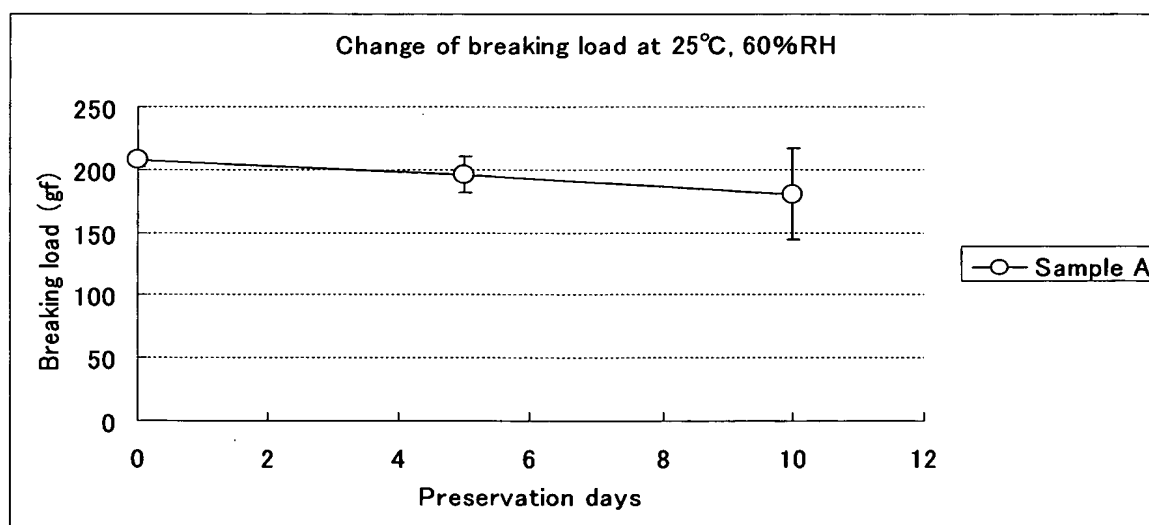


Fig. 3

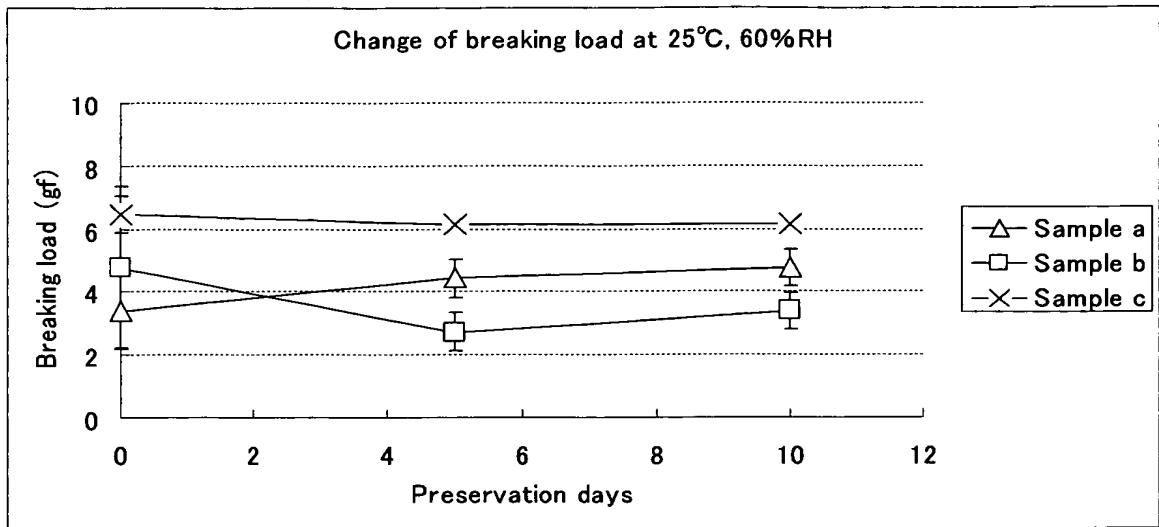


Fig. 4

5

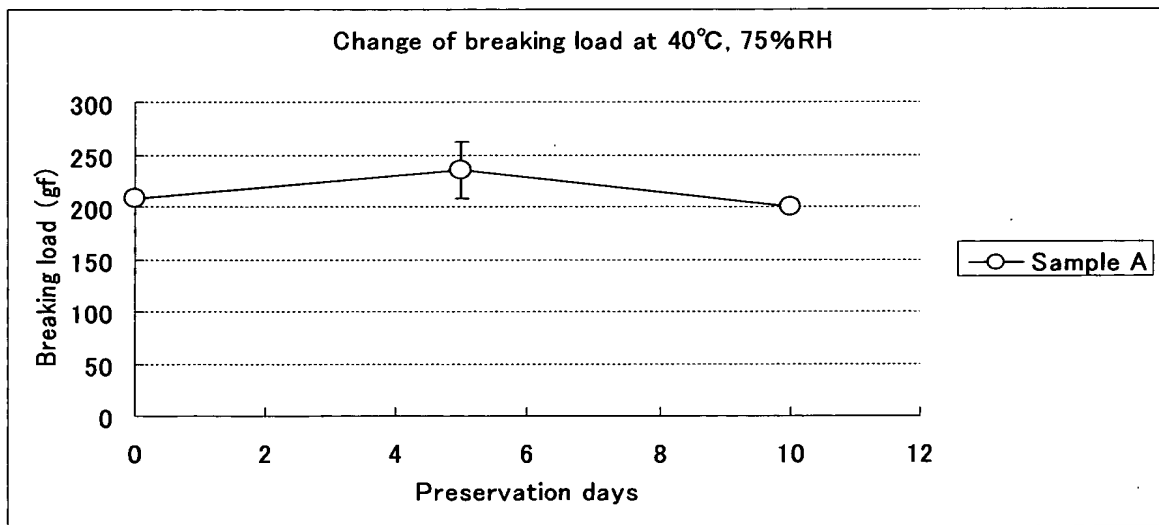


Fig. 5

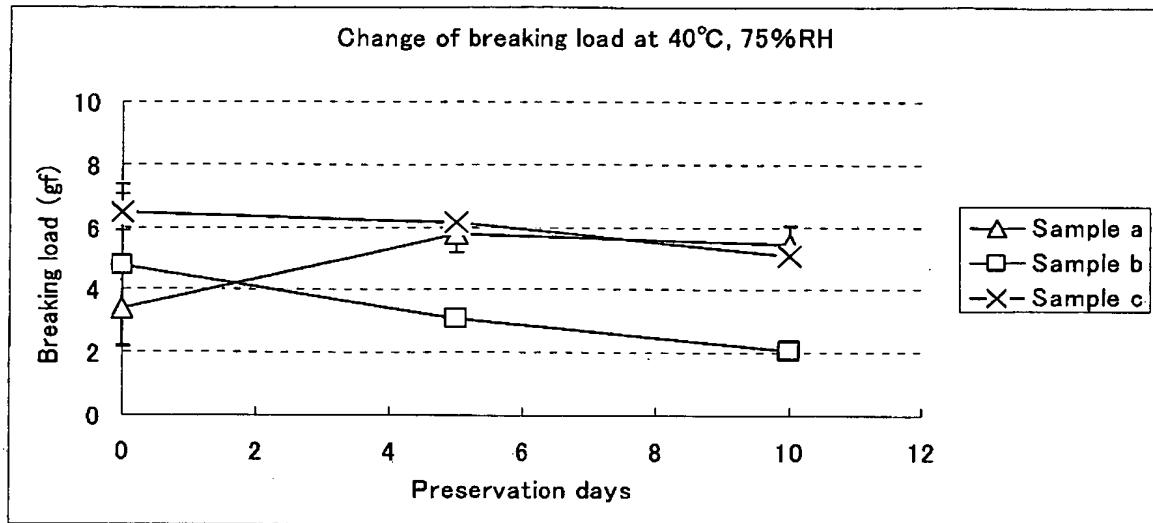


Fig. 6

5 The undersigned declares further that all statements made herein
of my own knowledge are true and that all statements made on
information and belief are believed to be true; and further that these
statements were made with the knowledge that willful false statements
and the like so made are punishable by fine or imprisonment, or both,
10 under Section 1001 of Title 18 of the United State Code and that such
willful false statements may jeopardize the validity of the above-
mentioned application or any patenting thereon.

This 7 of December, 2007

Tsunehiro Fukuchi

Tsunehiro FUKUCHI

20N

YAMADEN



SPAN

SAMPLE-

HC-3300

RE-3305

POWER
ON

